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PHENOTYPIC SPECTRUM OF DYSTROPHINOPATHIES IN SOUTH INDIAN CHILDREN: A CASE SERIES OF EIGHT PATIENTS

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ABSTRACT

Background: Dystrophinopathies comprise a spectrum of inherited neuromuscular disorders caused by mutations in the DMD gene, resulting in Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD). These disorders present with progressive muscle weakness and multisystem involvement including cardiac, respiratory, and neurocognitive manifestations.[12] **Objective:** To describe the clinical and phenotypic spectrum of dystrophinopathies in children presenting to a tertiary pediatric neurology center in South India. **Methods:** This retrospective case series included eight children evaluated for suspected dystrophinopathy. Clinical features, neurological findings, laboratory investigations including creatine kinase levels, and genetic results were reviewed. Phenotypic characteristics were analyzed to describe the clinical spectrum of disease. **Results:** Eight children (7 males, 1 female; age range 6 months–12 years) were included. The most common presenting manifestations were proximal muscle weakness, difficulty running, waddling gait, and positive Gowers' sign. Calf hypertrophy and markedly elevated serum creatine kinase levels were observed in several patients. Age at symptom onset ranged from infancy to late childhood. While most children demonstrated classical dystrophinopathy features, some exhibited atypical presentations including developmental delay and hypotonia in infancy. **Conclusion:** Dystrophinopathies in children demonstrate a wide clinical spectrum ranging from classical Duchenne muscular dystrophy to atypical and early-onset presentations. Recognition of these phenotypic variations is essential for early diagnosis and timely genetic confirmation.

KEYWORDS : Duchenne muscular dystrophy, Becker muscular dystrophy, dystrophinopathy, phenotypic spectrum, pediatric neurology

INTRODUCTION

Dystrophinopathies are a group of X-linked neuromuscular disorders caused by mutations in the dystrophin gene (DMD) located on chromosome Xp21.[8] The absence or deficiency of dystrophin leads to progressive muscle degeneration, resulting in Duchenne muscular dystrophy and Becker muscular dystrophy.[8]

Duchenne muscular dystrophy is the most severe form and typically presents in early childhood with delayed motor milestones, proximal muscle weakness, difficulty climbing stairs, and a positive Gowersign. Serum creatine kinase levels are markedly elevated, often exce-eding 10–20 times the upper limit of normal.[9]

Although dystrophinopathies primarily affect skeletal muscle, dystrophin is also expressed in the central nervous system, and its deficiency may lead to cognitive, behavioral, and neurodevelopmental abnormalities.[12] Studies have demonstrated alterations in brain structure and neurobehavioral function in patients with dystrophinopathies.[14]

The clinical presentation of dystrophinopathies can be heterogeneous, ranging from classical Duchenne muscular dystrophy to milder Becker phenotypes and atypical presentations that may mimic other neuromuscular disorders.[56] Rarely, symptomatic disease may also occur in females due to skewed X-chromosome inactivation.[7]

Understanding the phenotypic spectrum of dystrophinopathies in different populations is important for improving early diagnosis and clinical recognition.

This study aims to describe the clinical and phenotypic spectrum of dystrophinopathies in a cohort of South Indian children evaluated at a tertiary pediatric neurology center.

METHODS

This retrospective case series included children presenting to the pediatric neurology clinic with clinical suspicion of dystrophinopathy. Clinical data were collected from medical records including:

- age at presentation
- presenting symptoms
- neurological examination findings
- serum creatine kinase levels
- electrophysiological studies
- neuroimaging where available

Genetic testing results were reviewed where available to confirm the diagnosis.

RESULTS

Eight children with suspected dystrophinopathy were evaluated.

Demographic Characteristics: The cohort included seven male and one female patient, with ages ranging from 6 months to 12 years.

Clinical Presentation

The most common presenting features included:

- progressive proximal muscle weakness
- difficulty running or climbing stairs
- waddling gait
- positive Gowers'sign
- calf muscle hypertrophy

Two infants presented with generalized hypotonia and developmental delay, representing early-onset presentations.

Laboratory Findings

Serum creatine kinase levels were markedly elevated in several patients, with levels exceeding 15,000 IU/L in some cases, consistent with dystrophinopathy.

Elevated transaminases were also observed in some patients.

Phenotypic Comparison of Cases

Case	Age	Sex	Presenting Features	Neurological Findings	CK Level	Phenotypic Diagnosis
Case 1	10 yrs	Male	Difficulty running	Proximal weakness, ankle contractures	Mild elevation	Dystrophinopathy
Case 2	8 yrs	Male	Speech delay, gait difficulty	Calf hypertrophy	636 IU/L	Duchenne muscular dystrophy
Case 3	12 yrs	Male	Progressive weakness	Proximal weakness	Elevated	Dystrophinopathy
Case 4	7 yrs	Male	Difficulty walking	Positive Gowers sign	15,560 IU/L	Duchenne muscular dystrophy
Case 5	10 yrs	Male	Waddling gait	Gowers sign positive	16,630 IU/L	Becker muscular dystrophy
Case 6	10 yrs	Female	Limbgirdle weakness	Exercise intolerance	Elevated	Limbgirdle phenotype
Case 7	10 months	Male	Hypotonia	Developmental delay	—	Early-onset myopathy phenotype

Case 8	6 months	Male	Hypotonia	Flaccidity, feeding difficulty	—	Infantile hypotonia phenotype

DISCUSSION

This case series highlights the broad phenotypic spectrum of dystrophinopathies observed in children presenting with progressive muscle weakness.

The classical phenotype observed in several patients included proximal muscle weakness, Gowers 'sign, and calf hypertrophy, which are hallmark features of Duchenne muscular dystrophy.[8,9]

However, dystrophinopathies may also present with atypical phenotypes, including milder Becker muscular dystrophy or presentations mimicking other neuromuscular disorders.[5,9] Such variability may reflect differences in mutation type and dystrophin expression.

In addition to skeletal muscle involvement, dystrophin deficiency has been associated with cognitive and behavioral abnormalities, emphasizing the multisystem nature of the disorder.[1,2] Studies investigating brain involvement in dystrophinopathies have reported structural and functional abnormalities on neuroimaging and neuropsychological assessment.[1,2,4]

Although dystrophinopathies predominantly affect males, symptomatic disease has been reported in female patients due to skewed X-chromosome inactivation or chromosomal abnormalities, leading to variable phenotypic expression.[7]

The presence of early hypotonia and developmental delay in some patients in this cohort highlights the importance of considering dystrophinopathies in the differential diagnosis of infantile hypotonia and developmental delay.

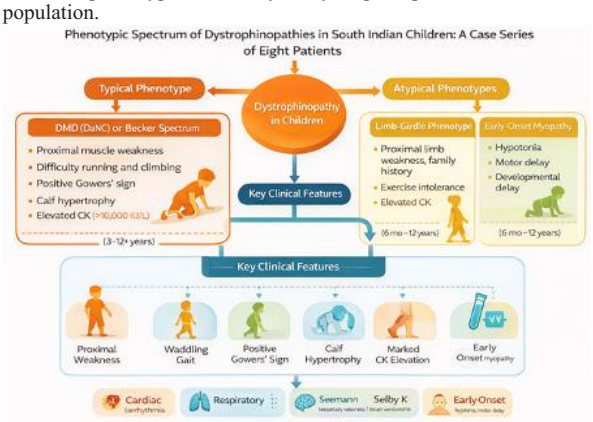
Early recognition of the clinical phenotype is essential to facilitate timely genetic testing, genetic counseling, and appropriate multidisciplinary management.

LIMITATIONS

The limitations of this study include:

- small sample size
- retrospective design
- incomplete longitudinal follow-up

Future studies involving larger cohorts are required to better characterize the phenotypic variability of dystrophinopathies in the Indian population.



CONCLUSION

Dystrophinopathies demonstrate a broad phenotypic spectrum in children, ranging from classical Duchenne muscular dystrophy to a typical and early-onset presentations. Recognition of these clinical variations is essential for early diagnosis and appropriate genetic evaluation.

REFERENCES

1. Colvin MK, Truba N, Sorensen S, Henricson E, Kinnett K. Dystrophinopathy and the brain: a Parent Project Muscular Dystrophy meeting report. Neuromuscul Disord. 2022;32(11):935-944.
2. Brain INvolvement in Dystrophinopathies (BIND): deep functional phenotyping of Duchenne muscular dystrophy and Becker muscular dystrophy patients.
3. Wang L, Jacoby E, Bell S, Stubbs D, Mayo P, Vilt M, et al. Molecular diagnosis of DMD-related dystrophinopathies using broad neuromuscular NGS panels. Genet Med Open. 2025;3:103050.
4. Social cognition in dystrophinopathies and neurodevelopmental disorders. Behavioural and psychophysiological measures. 2025.
5. Liewluck T, Tian X, et al. Dystrophinopathy mimicking metabolic myopathies. Neuromuscul Disord. 2015;25(8).
6. McMillan HJ, Darras BT. Atypical dystrophinopathy phenotypes. In: Swaiman's Pediatric Neurology. 2026.
7. Seemann N, Selby K, McAdam L, Biggar D, Kolski H, Goobie S, et al. Symptomatic dystrophinopathies in female children. Neuromuscul Disord. 2011;21(3):172-177.
8. Rae-Grant A, van Zuuren EJ, Valentine S. Duchenne and Becker muscular dystrophies. DynaMed. 2025.
9. Na SJ, Kim WJ, et al. Clinical, immunohistochemical, Western blot and genetic analysis in dystrophinopathy. J Clin Neurosci. 2013;20(8).
10. Defining outcome measures for behavioural and emotional problems in dystrophinopathies. 2024.